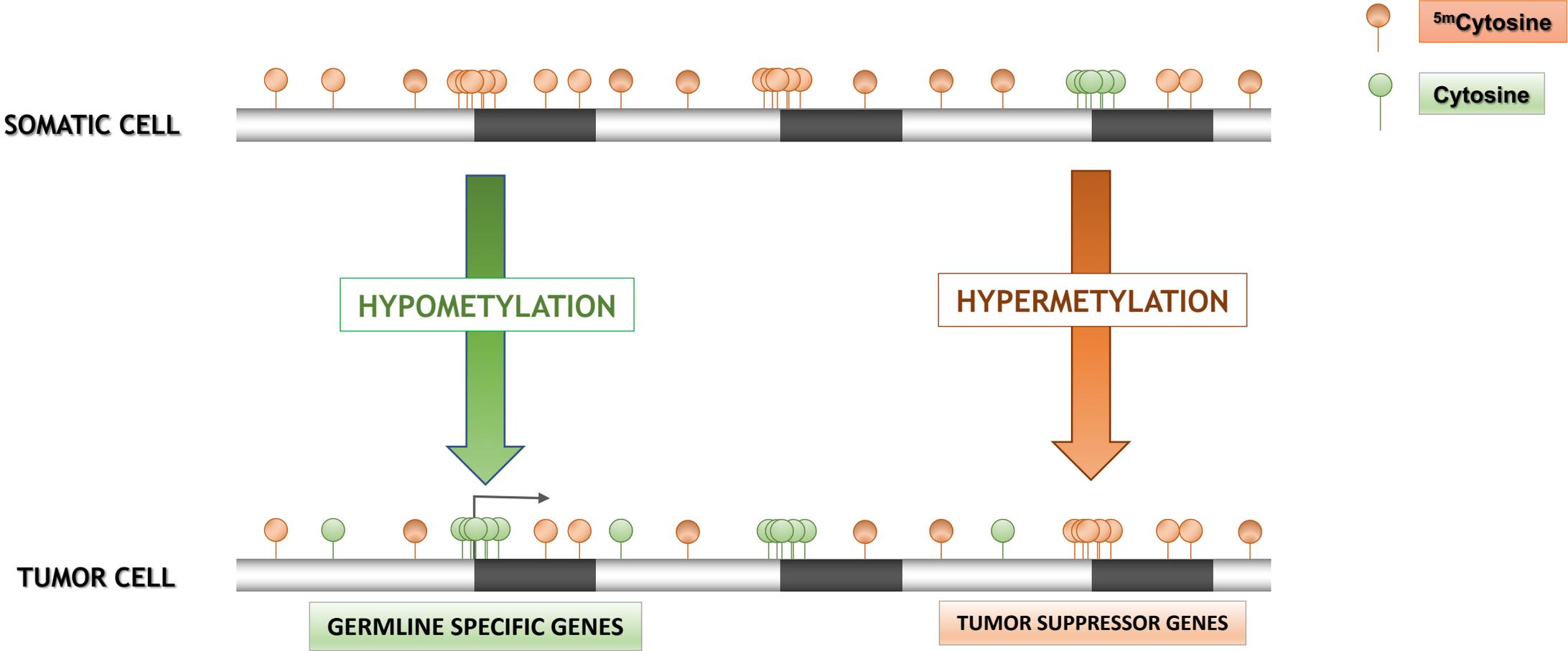


**Genome-wide approach to identify transcripts
induced by DNA demethylation in tumor cells**

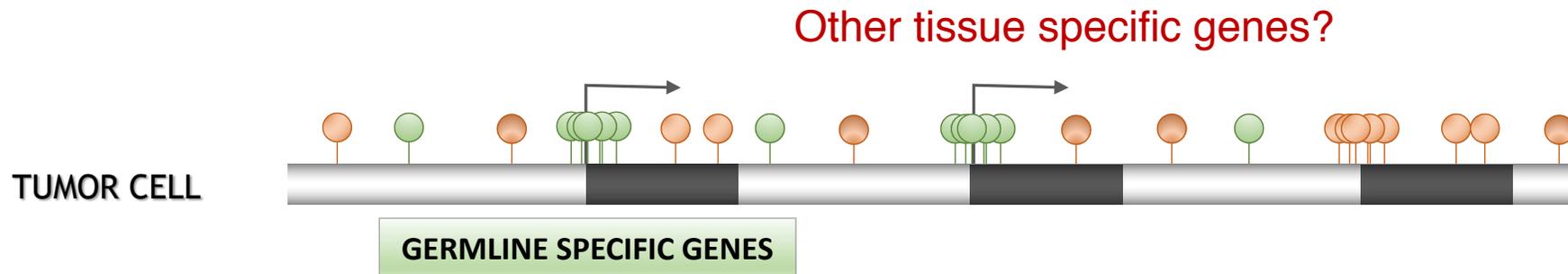
Axelle Lorient
Computational Biology and Bioinformatics
de Duve Institute

Methylation profiles are profoundly altered in cancer cells



Genome-wide approach to uncover the set of transcripts activated by DNA demethylation in tumors

- Other tissue specific genes reactivated by demethylation in tumors ?
- Tumor specific transcripts could be isoforms using demethylated alternative promoters



METHODOLOGY

OMICS CATALOGUE OF
LUNG ADENOCARCINOMA CELL LINES
Accession: PRJDB2256

26 LUAD cell lines

RNA-seq
fastq

hisat2

StringTie

*de novo transcript
assembling*

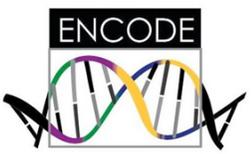
Bisulfite-seq
fastq

BisMark

Transcripts activated in cell lines
showing an inverse correlation between methylation and expression

Normal tissues

National Human Genome Research Institute



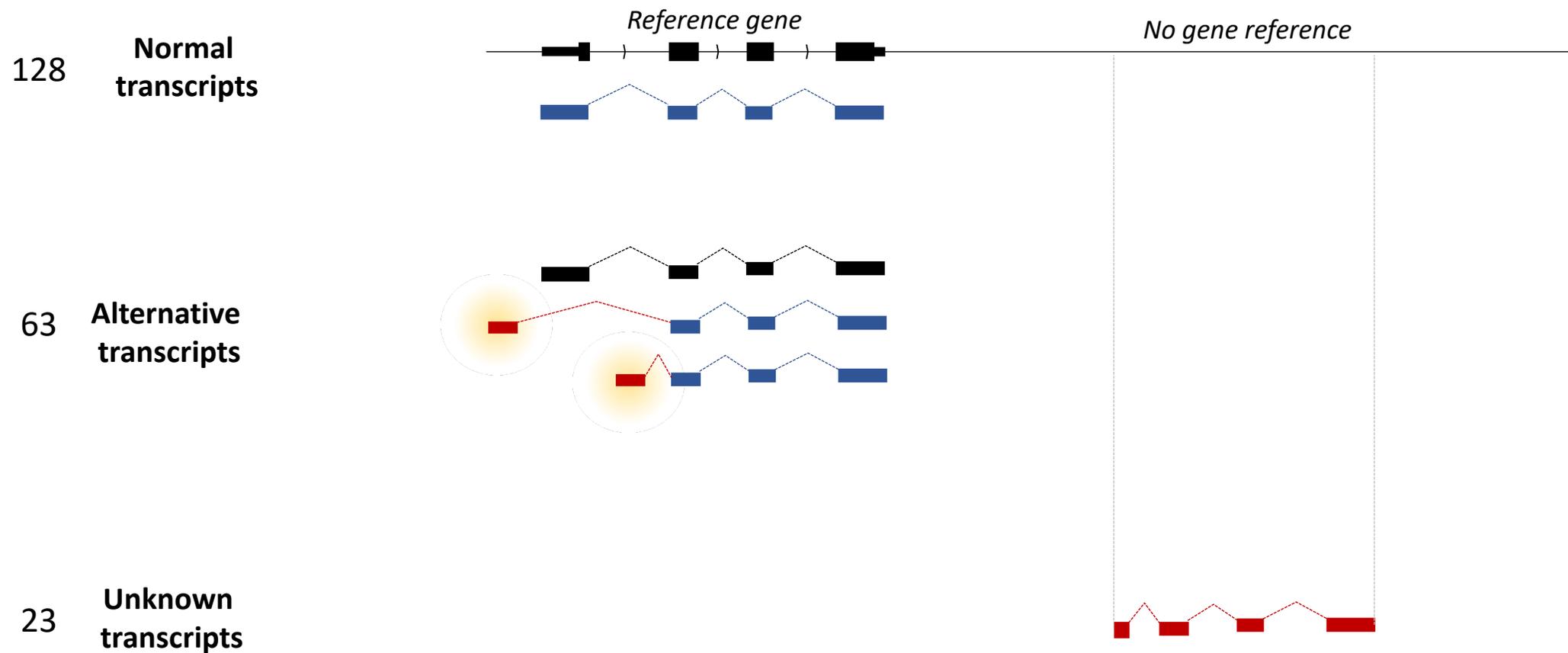
THE HUMAN
PROTEIN ATLAS

GTExPortal



- Tissue specificity analysis
- Methylation profile analysis

214 transcripts identified



AGO1: an example of alternative transcript activated by demethylation

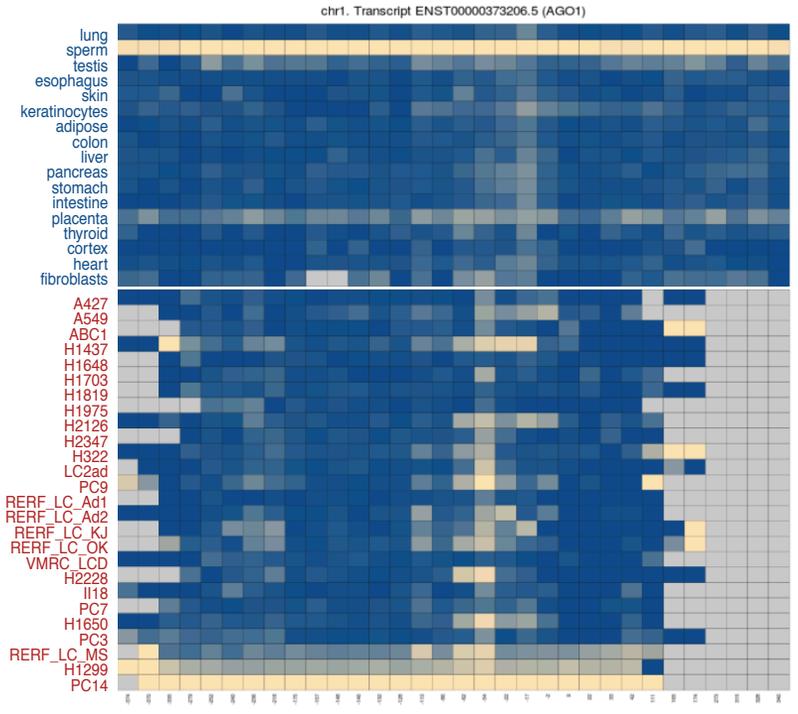
128 Normal transcripts

63 Alternative transcripts

23 Unknown transcripts

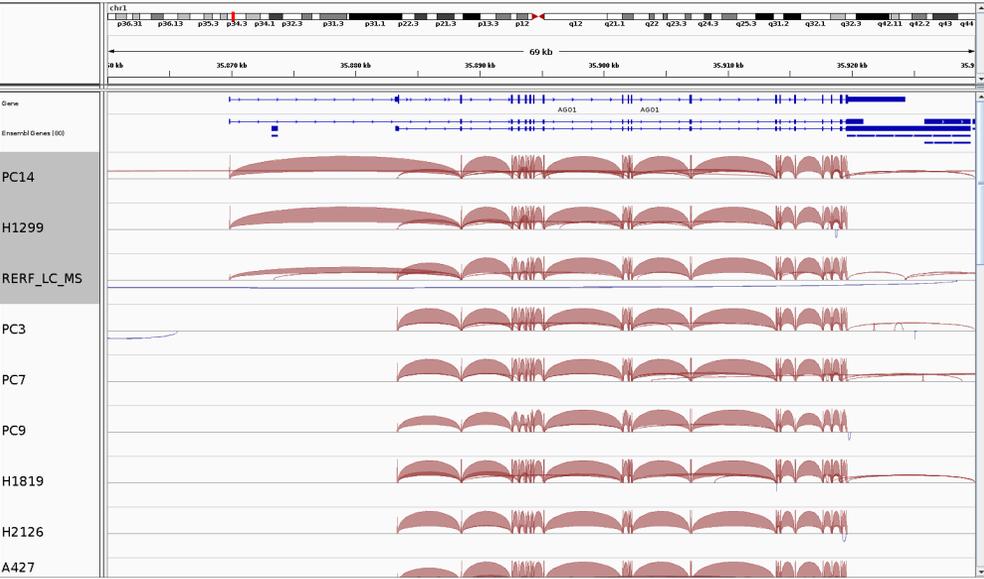
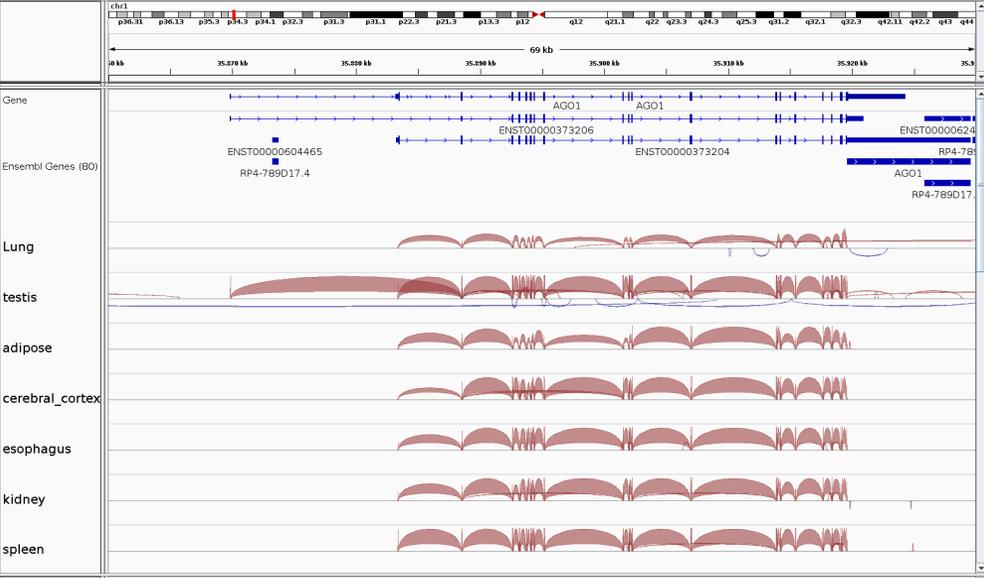
Normal tissues

Tumor cell lines



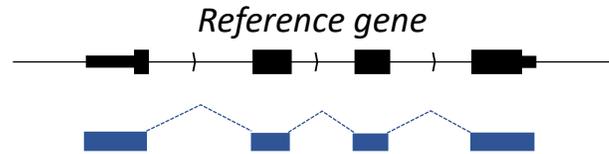
Normal tissues

Tumor cell lines

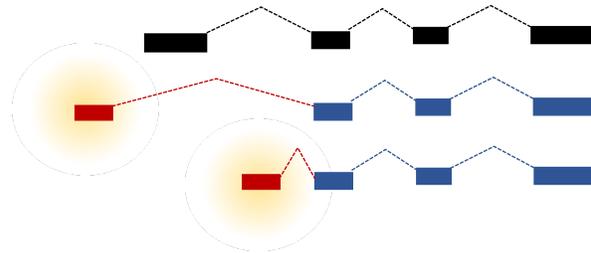


Tissue specificity

128 **Normal transcripts**



63 **Alternative transcripts**



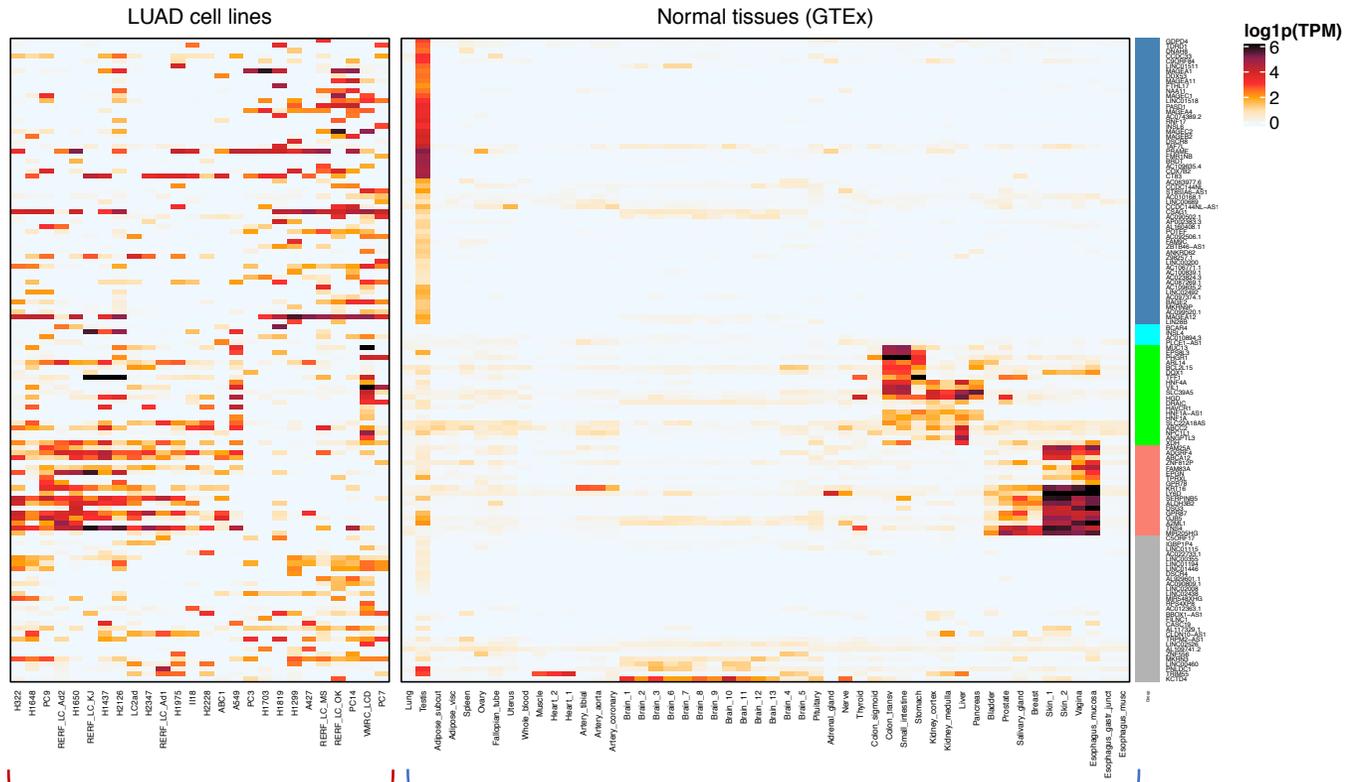
23 **Unknown transcripts**



RNAseq of 53 normal tissues
Multiple samples per tissues
Processed data only

=> Expression values are given at **Gene level**

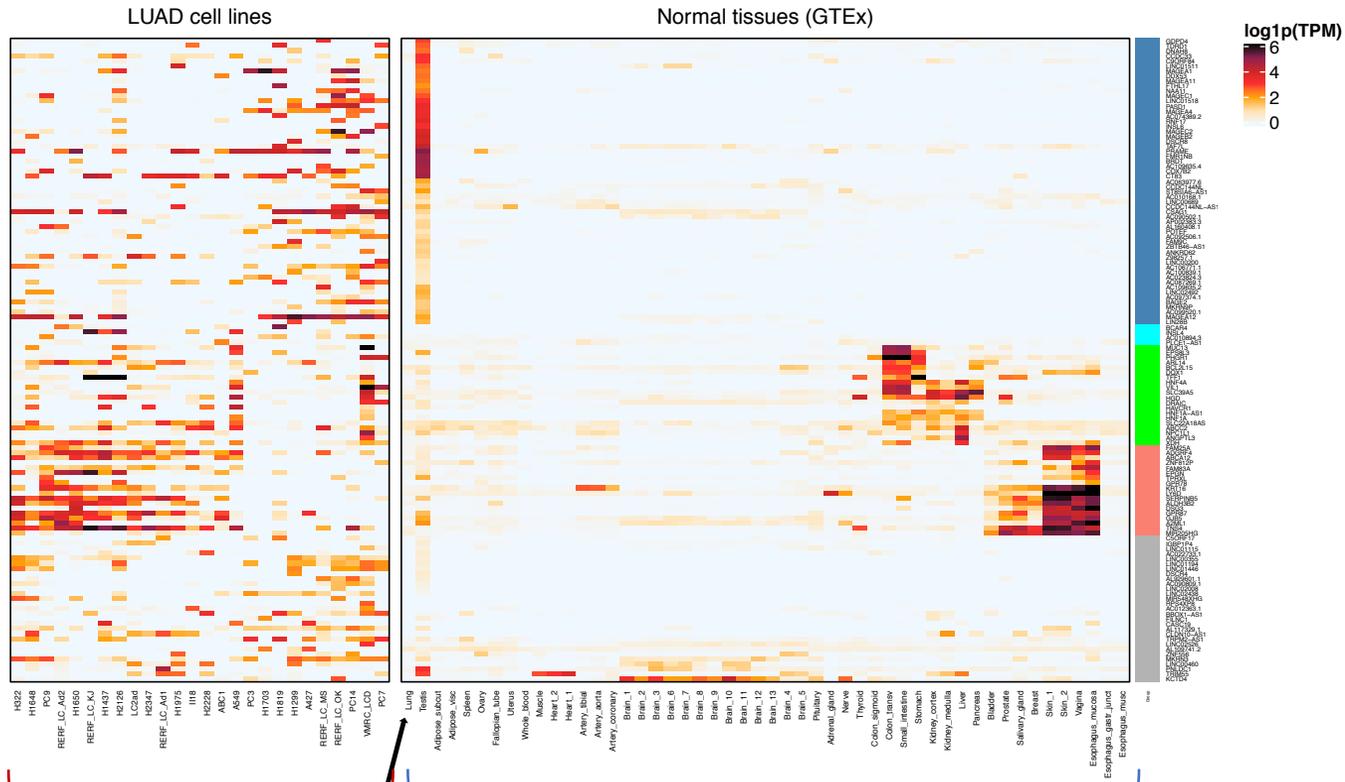
Tissue specificity



26 LUAD cell lines

50 normal tissues from Gtex

Tissue specificity

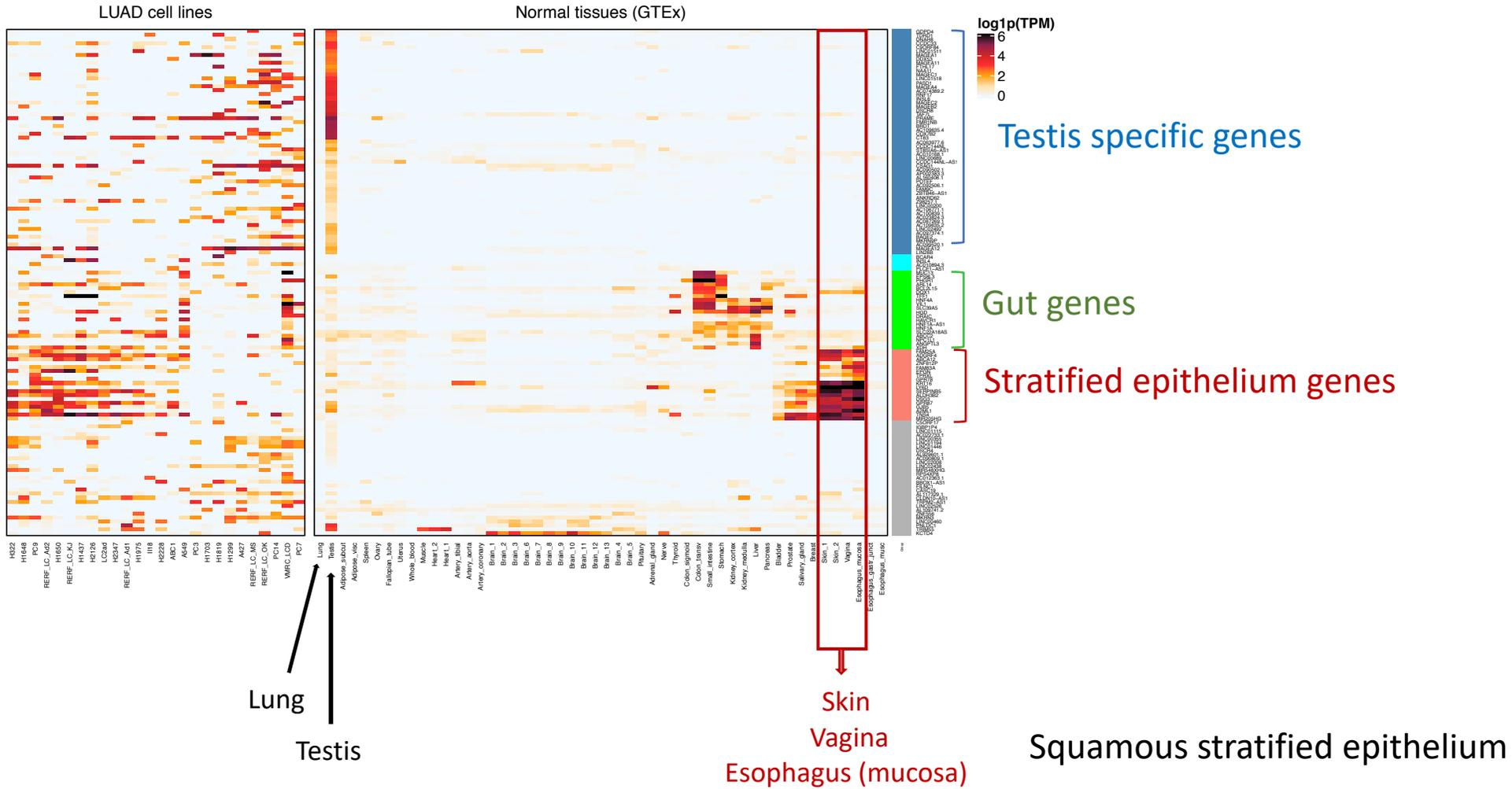


26 LUAD cell lines

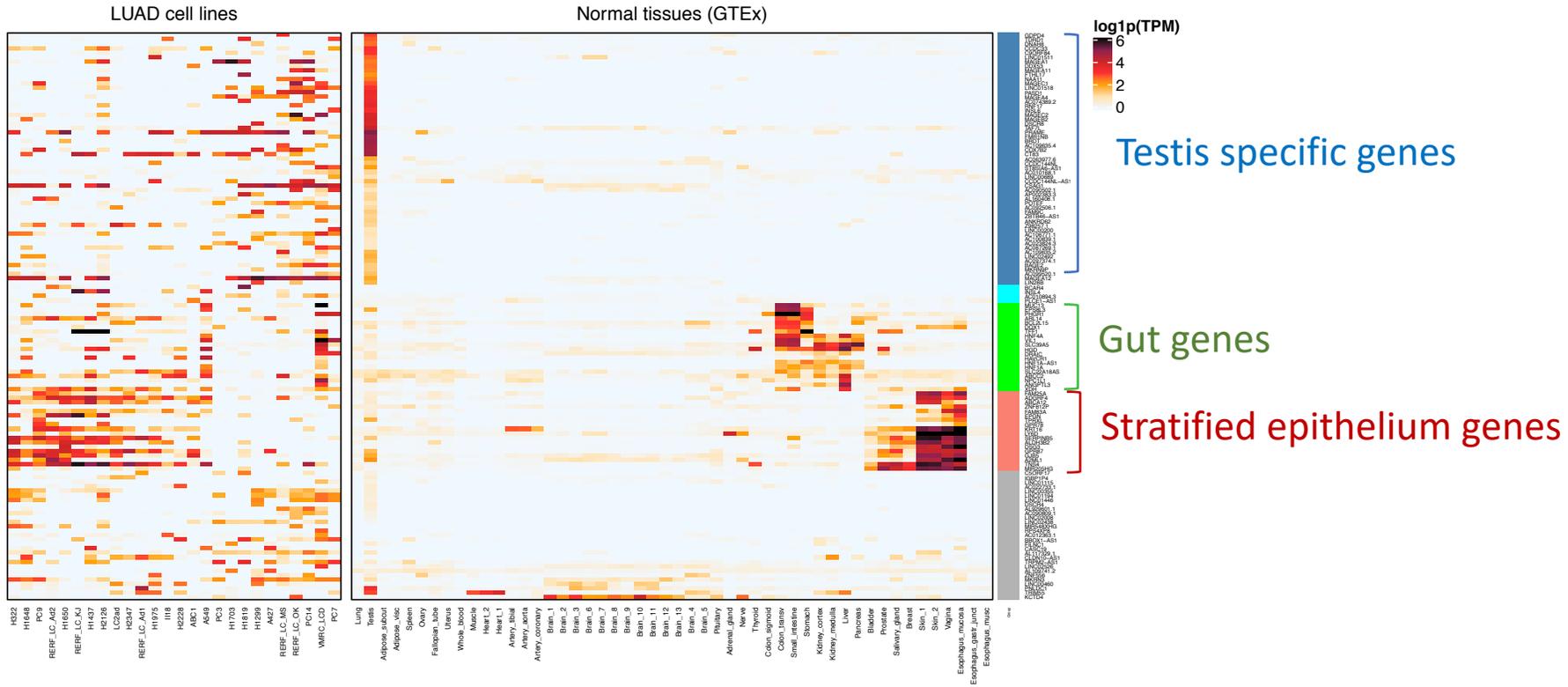
50 normal tissues from Gtex

Lung

Tissue specificity



Survival analyses

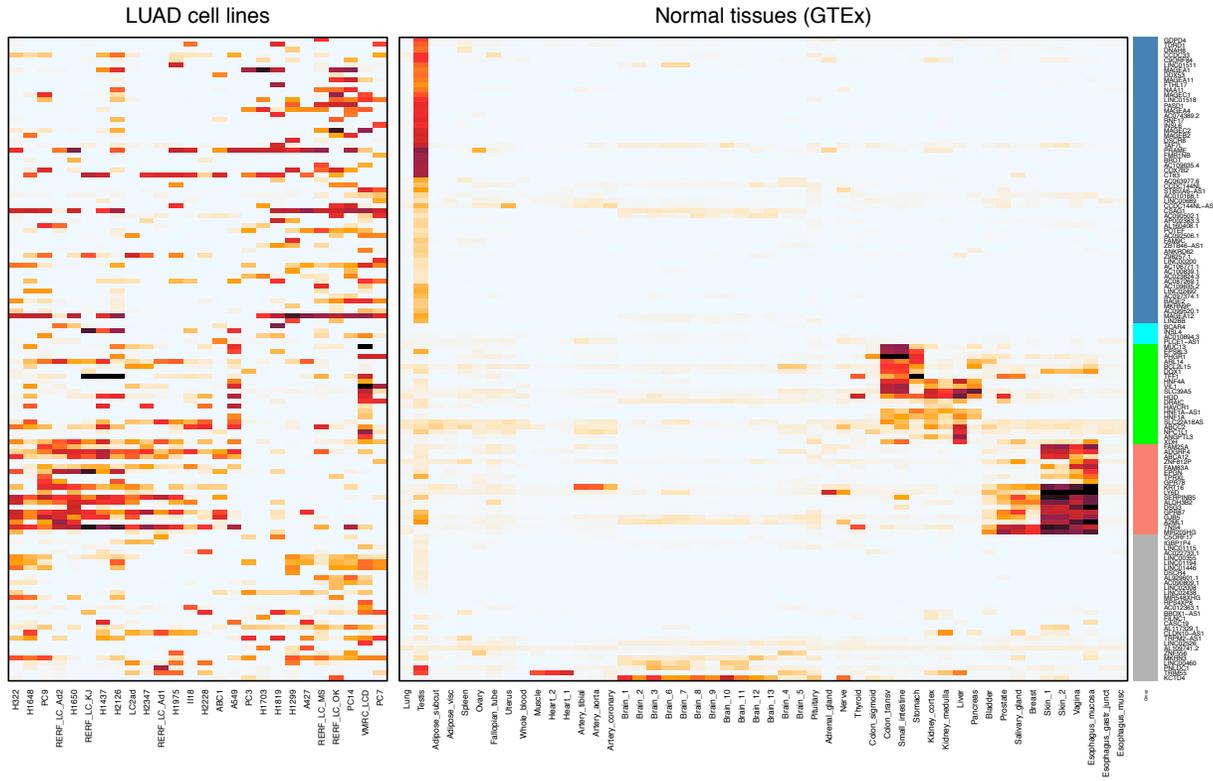


Is the activation of these genes in LUAD tumors associated to particular clinical features ?

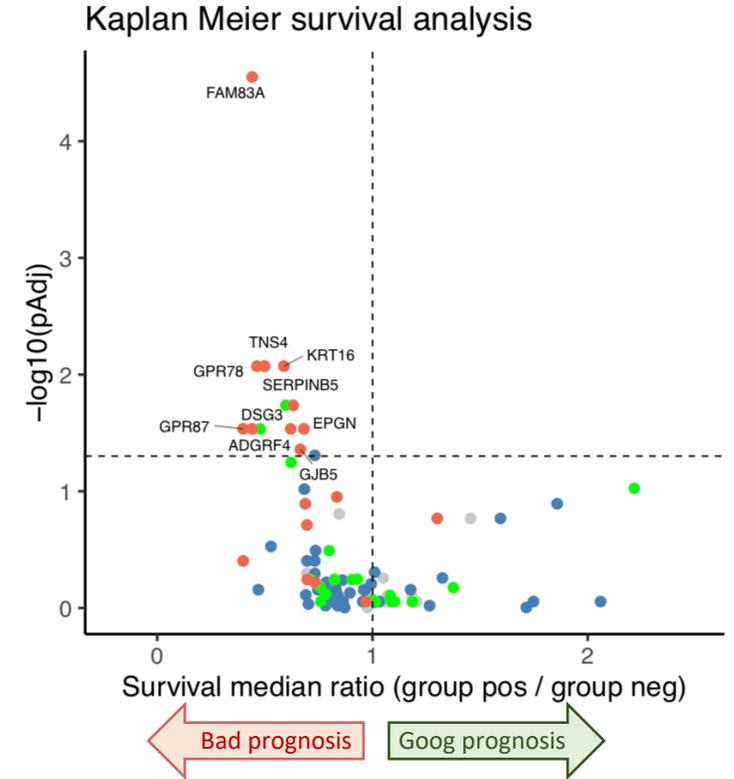
THE CANCER GENOME ATLAS
National Cancer Institute
National Human Genome Research Institute

- tumor Stage
- Tumor grade
- **Survival**

Survival analyses



Stratified
epithelium
genes



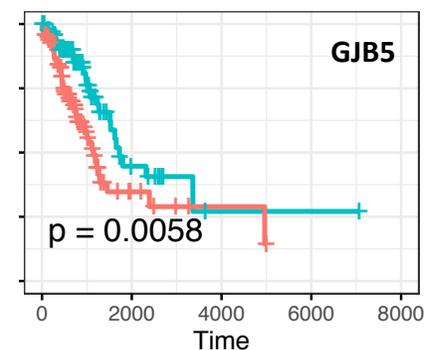
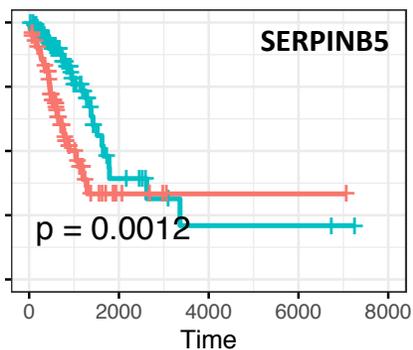
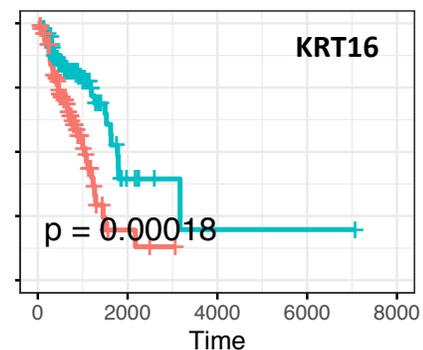
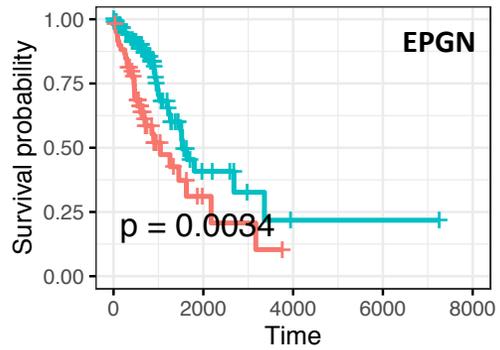
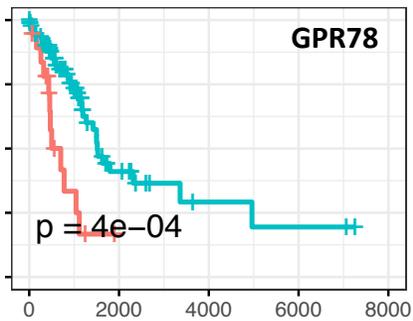
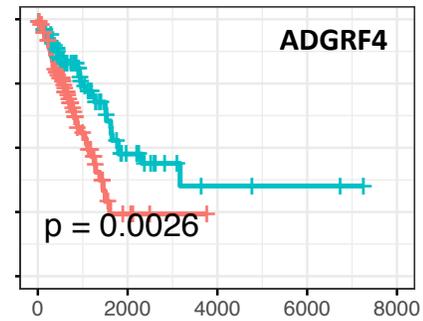
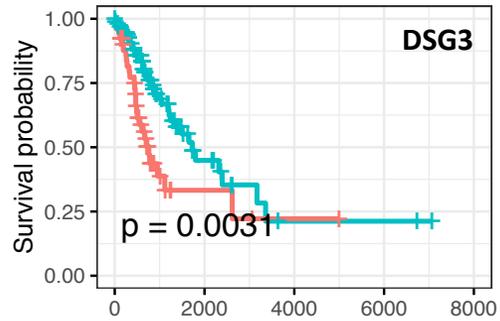
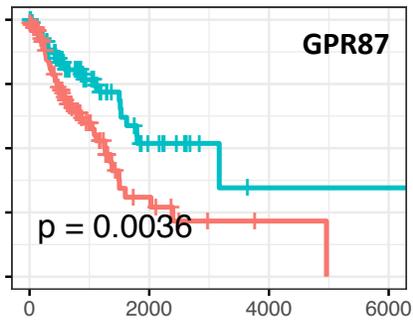
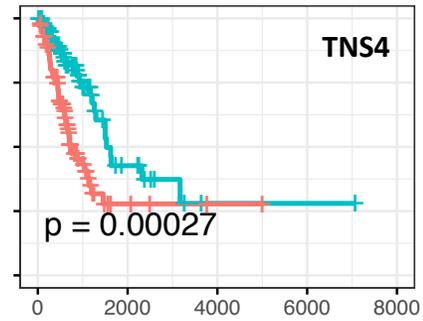
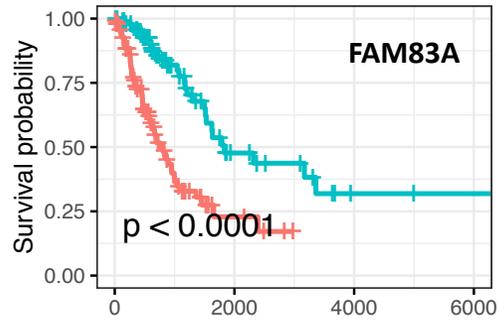
Is the activation of these genes in LUAD tumors associated to particular clinical features ?

- tumor Stage
- Tumor grade
- **Survival**

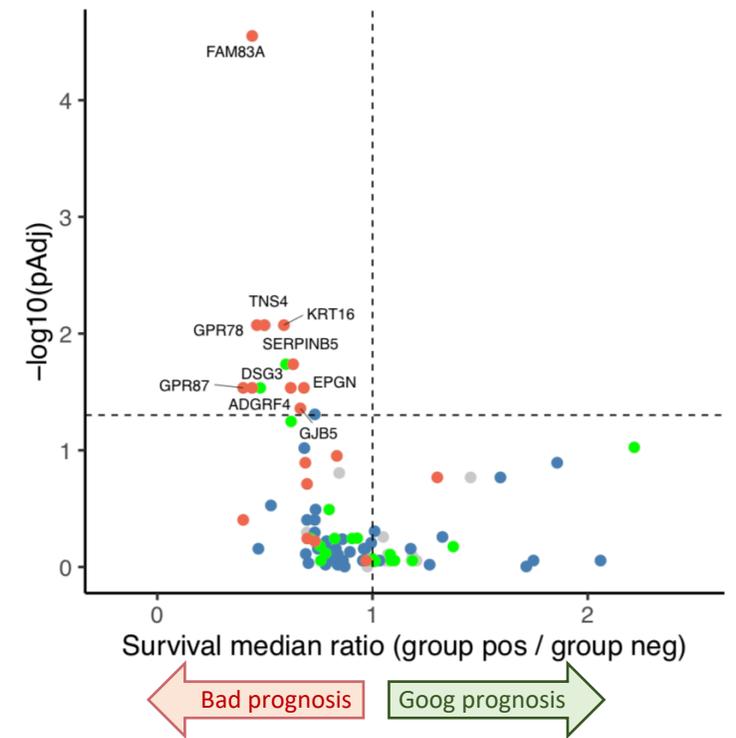
THE CANCER GENOME ATLAS
National Cancer Institute
National Human Genome Research Institute

Survival analyses

Strata + group=neg + group=pos

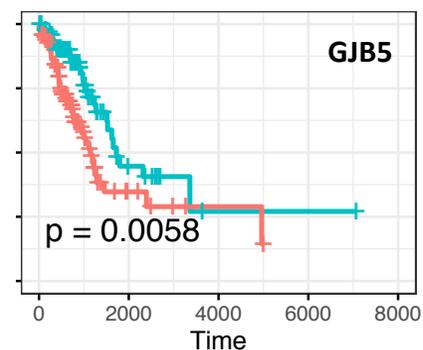
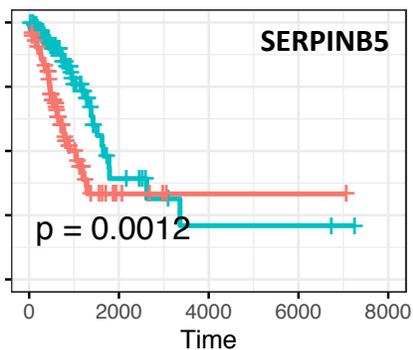
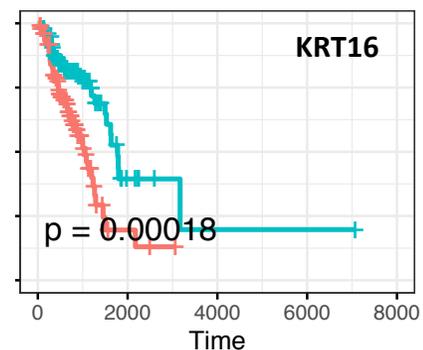
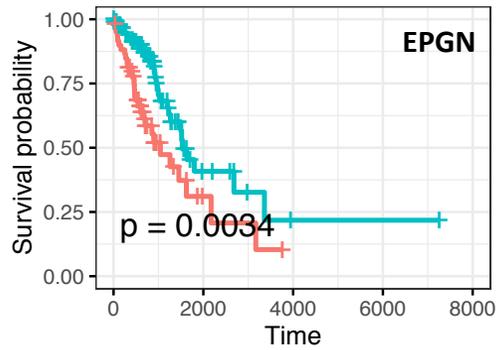
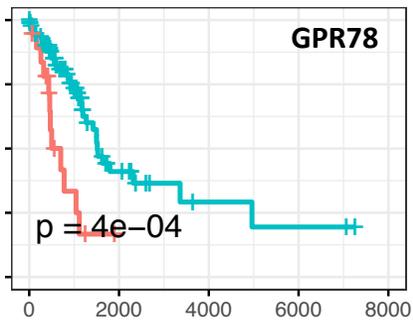
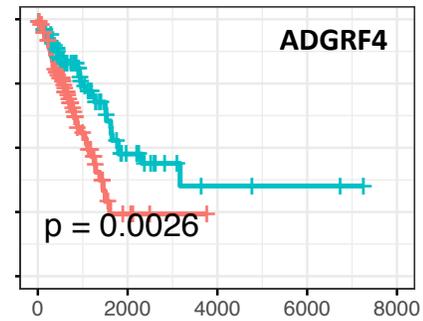
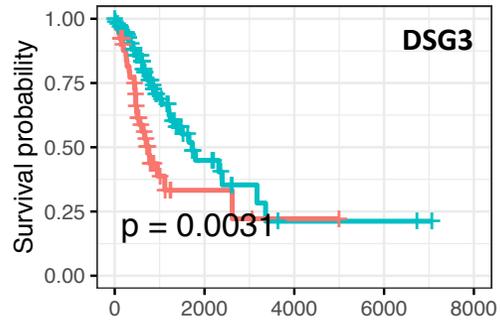
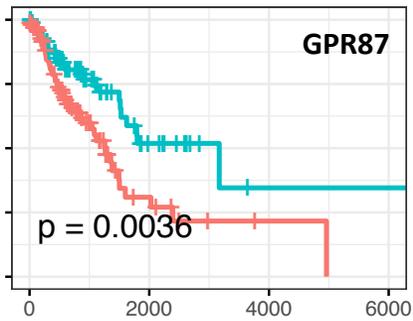
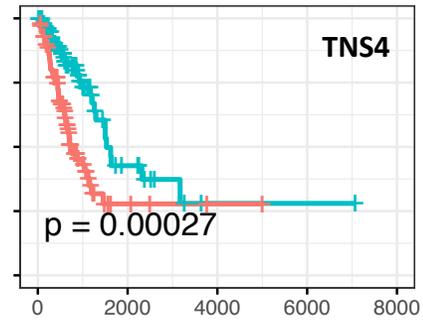
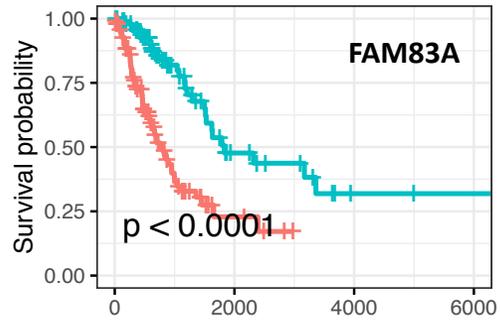


Kaplan Meier survival analysis

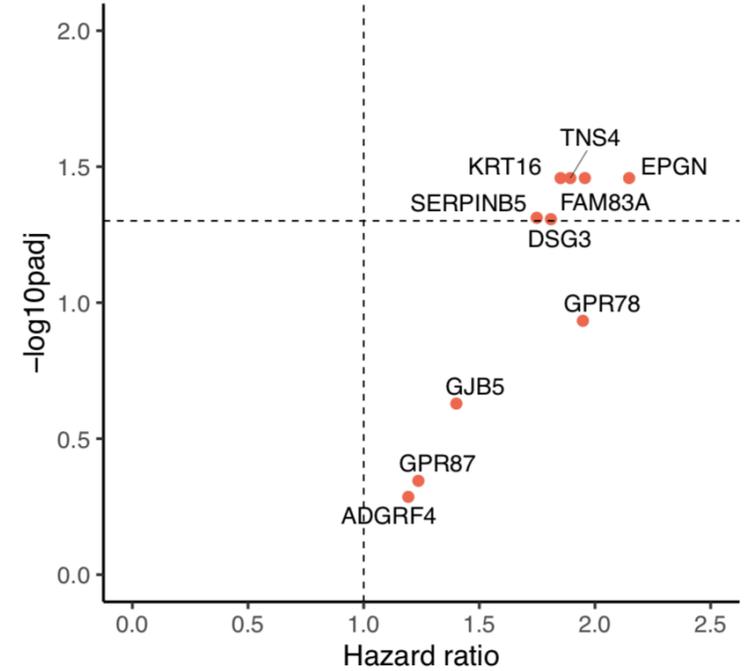


Survival analyses

Strata + group=neg + group=pos

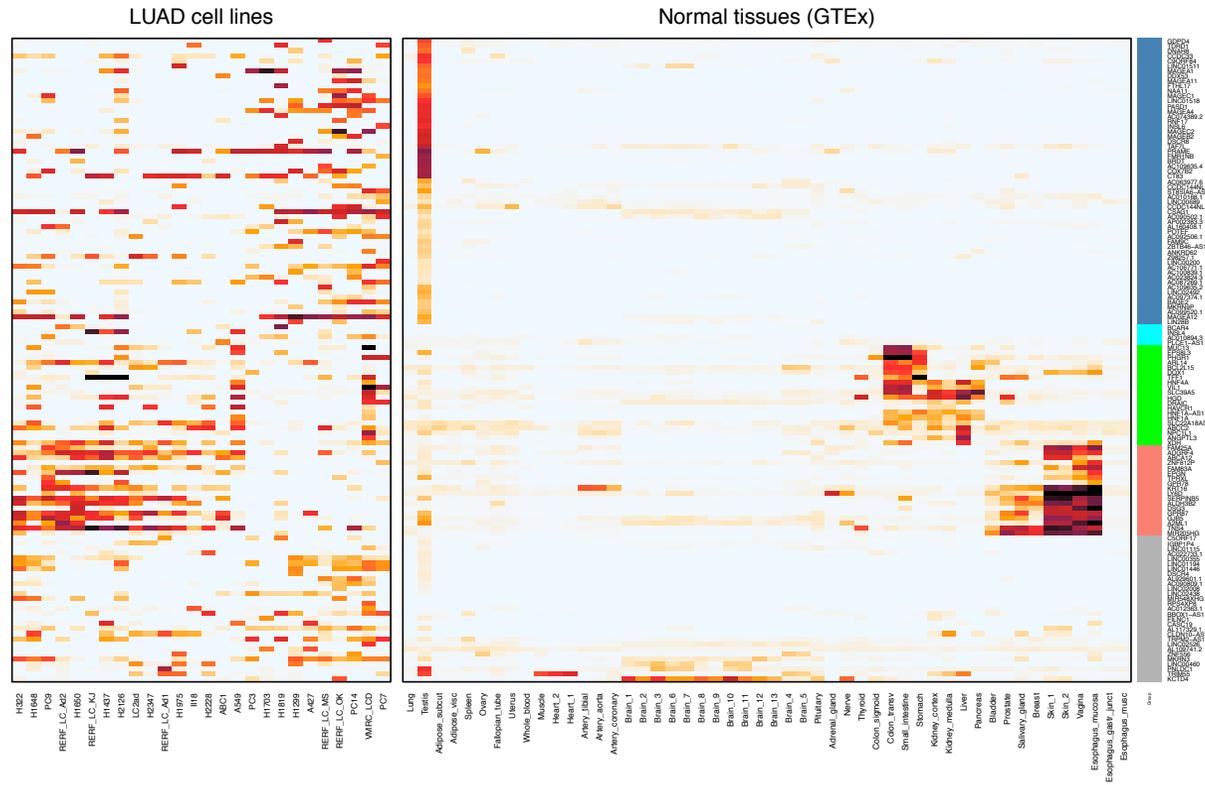


Cox model (+ stage and grade covariables)



← Goog prognosis → Bad prognosis

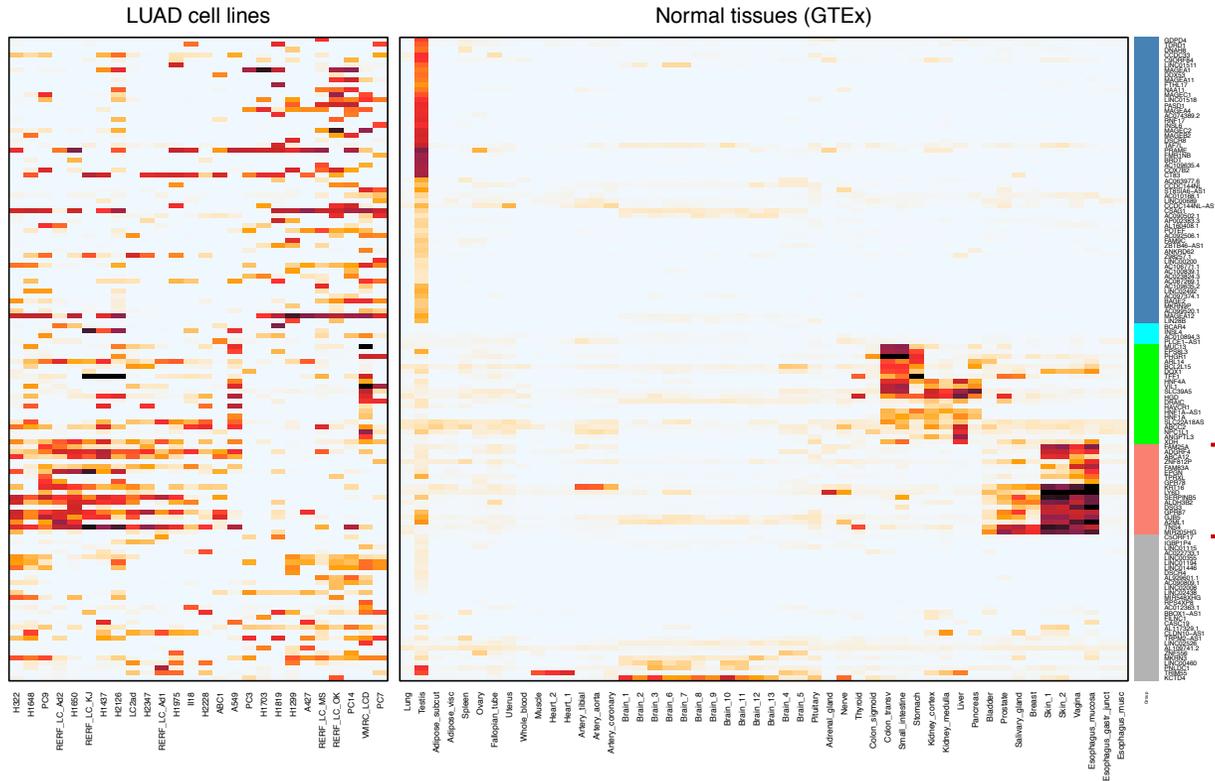
CONCLUSION



Stratified epithelium genes

- Associated to bad prognosis
- Prognosis biomarkers
- Oncogenic functions ?

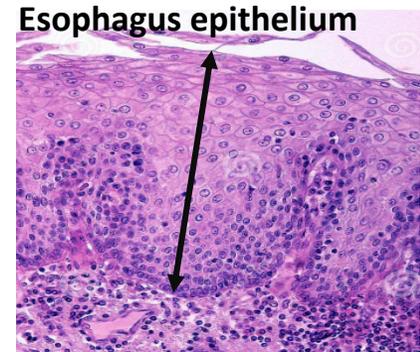
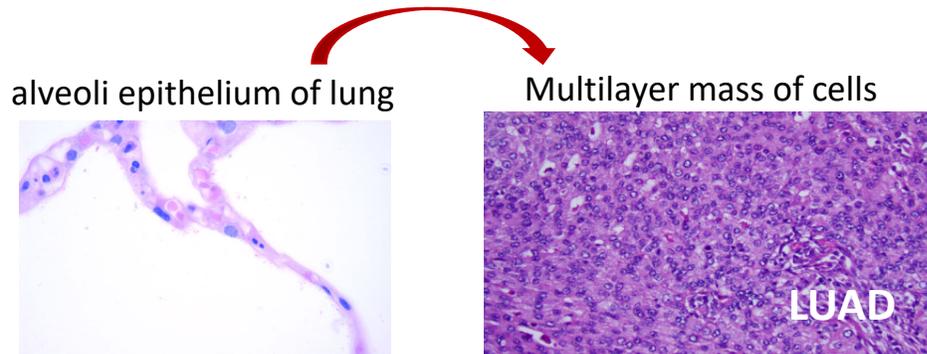
CONCLUSION



Stratified epithelium genes

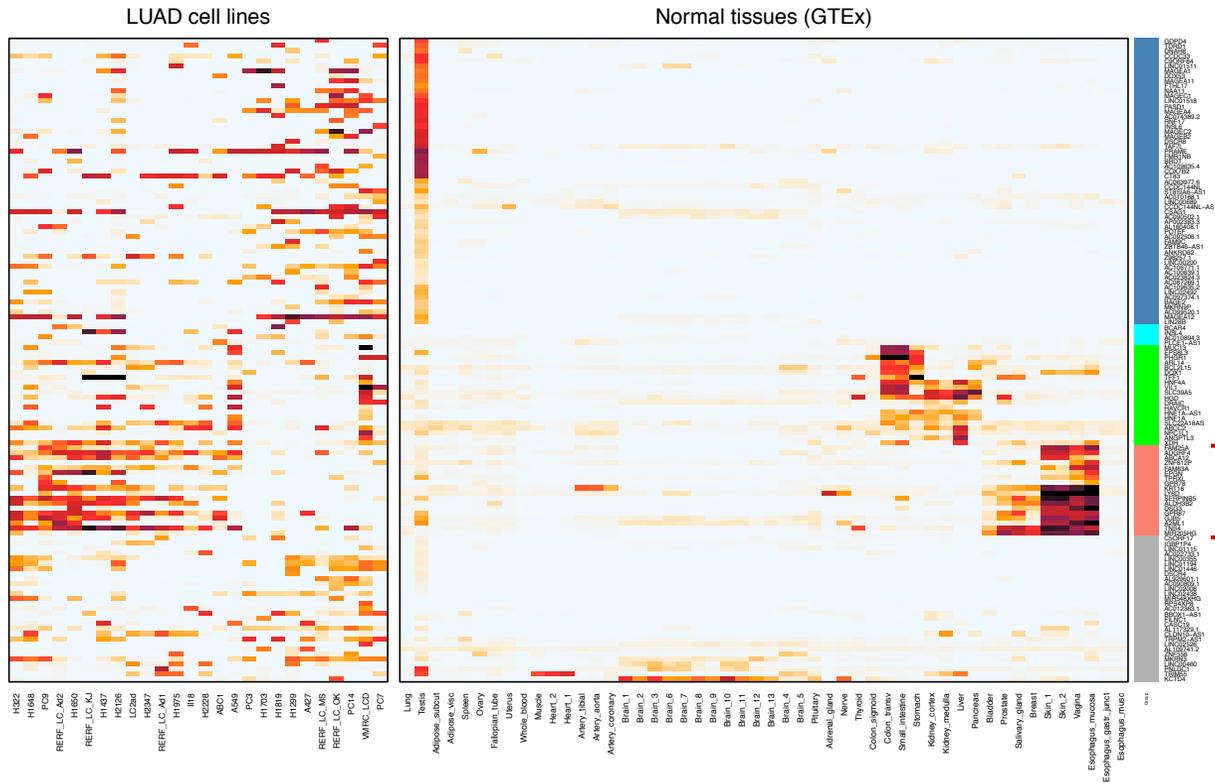
- Associated to bad prognosis
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Activation of "stratification" genes ?



squamous stratified epithelium

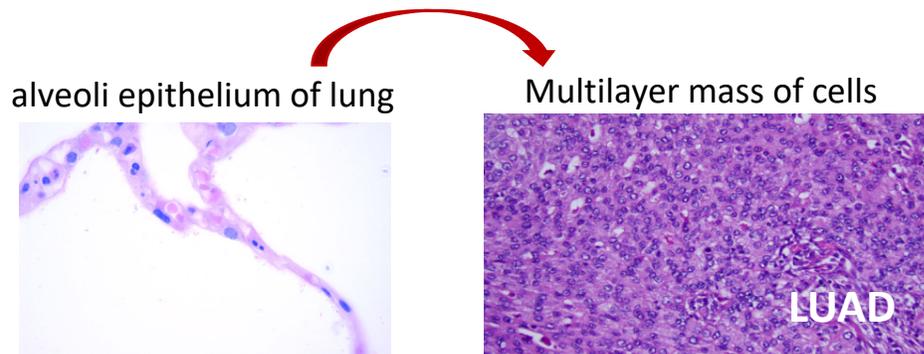
CONCLUSION



Stratified epithelium genes

- Associated to bad prognosis
- Prognosis biomarkers
- Oncogenic functions ?

Activation of “stratification” genes ?



Preliminary results:

Other epithelium stratified genes are also activated in LUAD tumors by a mechanism independent of DNA methylation

- « Stratification » gene signature in LUAD tumors ?

Pr Charles De Smet
Anna Diacofotakis

Genetics and Epigenetics Unit
De Duve Institute
belgium

Pr Laurent Gatto

Computational Biology and Bioinformatics
de Duve Institute

